

CLAIMS

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- 5 1. A composition useful in the treatment of pathological conditions characterized by neovascularization comprising an immunoconjugate protein constructed as a dimer of two identical chains, each having an effector domain which is the Fc region of an IgG1 immunoglobulin conjugated to a targeting domain which is a mutant form of factor VII that binds to tissue factor but does not initiate blood coagulation.
2. A composition according to claim 1 wherein the targeting domain of the immunoconjugate protein comprises human factor VII having a substitution of alanine for lysine-341.
3. A composition according to claim 1 wherein the targeting domain of the immunoconjugate protein comprises human factor VII having a substitution of alanine for serine-344.
4. A composition according to claim 1 further comprising a second immunoconjugate protein constructed as a dimer of two identical chains, each having an effector domain which is the Fc region of a human IgG1 immunoglobulin conjugated to a targeting domain which is a human scFv or V_H antibody fragment that binds to neovasculature.
5. A composition according to claim 1 further comprising a second immunoconjugate protein constructed as a dimer of two identical chains, each having an effector domain which is the Fc region of an IgG1 immunoglobulin conjugated to a targeting domain which is a scFv or V_H antibody fragment that binds to a particular type of tumor cell.
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6. A composition according to any of claims 1 to 5 wherein the immunoconjugate protein is encoded as a secreted molecule in an expression vector.

7. A composition according to claim 6 wherein the expression vector is a replication-deficient adenoviral vector.

8. A composition according to claim 6 wherein the expression vector is an adeno-associated expression vector.

SUB AS

9. A method for treating a disease associated with neovascularization, which comprises administering to a patient having the disease an effective amount of at least one type of immunoconjugate protein comprising the Fc region of an IgG1 immunoglobulin conjugated to a targeting domain comprising a mutant form of factor VII that binds to tissue factor but does not initiate blood clotting.

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10. A method according to claim 9 wherein the targeting domain of the immunoconjugate protein comprises human factor VII having a substitution of alanine for lysine-341.

11. A method according to claim 9 wherein the targeting domain of the immunoconjugate protein comprises human factor VII having a substitution of alanine for serine-344.

12. A method according to claim 9 wherein a second immunoconjugate protein having an effector domain which is the Fc region of an IgG1 immunoglobulin conjugated to a targeting domain which is a human scFv or V_H antibody fragment that binds to neovasculature or to tumor cells is administered to the patient as adjunct therapy.

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SUB AS

13. A method according to claim 9 which is a treatment for a disease selected from the group consisting of cancer involving a vascularized tumor, rheumatoid arthritis, and the exudative form of macular degeneration.

14. A method according to any of claims 9 to 13 wherein the patient is treated by administration of an immunoconjugate protein in a pharmaceutically acceptable carrier.

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15. A method according to any of claims ~~9~~ to 13 wherein the patient is treated by administration of a replication-deficient adenoviral vector or an adeno-associated vector carrying a cDNA encoding a secreted form of one or more types of immunoconjugate protein.

16. A method according to claim 15 wherein a replication-deficient adenoviral vector is employed.

17. A method for treating cancer in a patient, which comprises administering to the patient an effective amount of at least one type of immunoconjugate protein comprising the Fc region of a human IgG1 immunoglobulin conjugated to a targeting domain comprising a mutant form of human factor VII selected from the
5 group consisting of native factor VII having a substitution of alanine for lysine-341, native factor VII having a substitution of alanine for serine-344, and mixtures thereof.

18. A method according to claim 17 wherein a second immunoconjugate protein having an effector domain which is the Fc region of a human IgG1 immunoglobulin conjugated to a targeting domain which is a human scFv or V_H antibody fragment that binds to the patient's type of tumor cell is administered to the patient as adjunct therapy.

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19. A method according to claims 17 or 18 wherein the patient is treated by administering the immunoconjugate in a pharmaceutically acceptable carrier.

20. A method according to claims 17 or 18 wherein the patient is treated by administering a replication-deficient adenoviral vector carrying a cDNA encoding a secreted form of one or more types of the immunoconjugate protein.

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